

<b>TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A SUBMISSION UNDER 35 U.S.C. 371</b>		ATTORNEY'S DOCKET NUMBER <b>06189/HG</b>
INTERNATIONAL APPLICATION NO. <b>PCT/JP2004/016715</b>	INTERNATIONAL FILING DATE <b>4 NOVEMBER 2004</b>	U.S. APPLICATION NO. (If known, see 37 CFR 1.5) <b>10/577,982</b>
TITLE OF INVENTION <b>METHOD OF DETECTING GENETIC POLYMORPHISM</b>		PRIORITY DATE CLAIMED <b>7 NOVEMBER 2003; 16 APRIL 2004</b>
APPLICANT(S) FOR DO/EO/US <b>Makoto KOIZUMI</b>		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<ol style="list-style-type: none"> <li>1. <input type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a submission under 35 U.S.C. 371.</li> <li>2. <input checked="" type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a submission under 35 U.S.C. 371.</li> <li>3. <input type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.</li> <li>4. <input type="checkbox"/> The US has been elected (Article 31).</li> <li>5. <input type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))               <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input type="checkbox"/> has been communicated by the International Bureau.</li> <li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li> </ol> </li> <li>6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).               <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> is attached hereto.</li> <li>b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).</li> </ol> </li> <li>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))               <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).</li> <li>b. <input type="checkbox"/> have been communicated by the International Bureau.</li> <li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d. <input type="checkbox"/> have not been made and will not be made.</li> </ol> </li> <li>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</li> <li>9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</li> <li>10. <input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</li> </ol>		
<b>Items 11 to 20 below concern document(s) or information included:</b>		
<ol style="list-style-type: none"> <li>11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</li> <li>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</li> <li>13. <input type="checkbox"/> A preliminary amendment.</li> <li>14. <input type="checkbox"/> An Application Data Sheet under 37 CFR 1.76.</li> <li>15. <input type="checkbox"/> A substitute specification.</li> <li>16. <input type="checkbox"/> A power of attorney and/or change of address letter.</li> <li>17. <input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821- 1.825.</li> <li>18. <input type="checkbox"/> A second copy of the published International Application under 35 U.S.C. 154(d)(4).</li> <li>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).</li> <li>20. <input type="checkbox"/> Other items or information:</li> </ol>		

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Dorothy DeFrancesco

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U.S. APPLICATION NO. (if known, see 37 CFR 1.5) <b>10/577,982</b>		INTERNATIONAL APPLICATION NO. <b>PCT/JP2004/016715</b>		ATTORNEY'S DOCKET NUMBER <b>06189/HG</b>	
The following fees have been submitted				<b>CALCULATIONS</b>	<b>PTO USE ONLY</b>
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23. <input type="checkbox"/> Search fee Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority..... \$100 International Search Report prepared and provided to the Office..... \$400 All other situations..... \$500				\$	
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<p>SEND ALL CORRESPONDENCE TO:</p> <p><b>CUSTOMER NO. 01933</b></p> <p>Richard S. Barth Frishauf, Holtz, Goodman &amp; Chick P.C. 220 5TH AVE FL 16 NEW YORK NY 10001-7708</p>					
				<p></p> <p>SIGNATURE</p> <p><b>Richard Barth</b></p> <p>NAME</p> <p><b>28,180</b></p> <p>REGISTRATION NUMBER</p>	

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**IN THE UNITED STATES PATENT  
AND TRADEMARK OFFICE**

Applicant(s): Makoto KOIZUMI  
Serial No. : 10/577,982  
Docket No. : 06189/HG  
Filed : May 2, 2006  
For : METHOD OF DETECTING GENETIC  
POLYMORPHISM  
Customer No.: 01933

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Paper to Account No. 06-1378.

This application is a United States national phase  
application under 35 USC 371 of International application  
PCT/JP2004/016715.

Submitted herewith are the following:

- (1) a copy of the International Search Report for  
PCT/JP2004/016715;
- (2) copies of publications cited in the aforesaid  
International Search Report;
- (3) copies of publications disclosed on pages 2 to 6 of the  
present specification; and
- (4) Forms PTO/SB/08A and PTO/SB/08B.

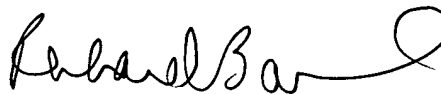
Each of the publications cited in said International Search Report is considered relevant or material to the patentability of the present invention, in view of the citation thereof in said Search Report.

Said International Search Report is in English, thereby satisfying the requirements for a concise explanation of relevance for the publications cited therein.

It is respectfully requested that initialed copies of the enclosed Forms PTO/SB/08A and PTO/SB/08B be returned to the undersigned to indicate that the publications listed therein have been considered and made of record.

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& Chick, P.C.  
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RSB/ddf

Respectfully submitted,



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Richard S. Barth  
Reg. No. 28,180

- Encs.: (1) Copy of International Search Report  
for PCT/JP2004/016715
- (2) Forms PTO/SB/08A and PTO/SB/08B
- (3) Copies of the publications cited on said  
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PTO/SB/08A (08-00)

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for Form 1449A/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				Application Number	10/577,982
				Filing Date	May 2, 2006
				First Named Inventor	Makoto KOIZUMI
				Group Art Unit	
				Examiner Name	
Sheet	1	of	3	Attorney Docket Number	06189/HG

## U.S. PATENT DOCUMENTS

Exam. Inits <sup>1</sup>	Cite No <sup>1</sup>	Document Number	Kind Code <sup>2</sup>	Name of Patentee or Applicant	Publication Date MM-DD-YYYY	Relevant Portion

## FOREIGN PATENT DOCUMENTS

Exam. Inits <sup>1</sup>	Cite No <sup>1</sup>	offc <sup>3</sup>	Document Number <sup>4</sup>	Kind Code <sup>5</sup>	Name of Patentee or Applicant	Publication Date MM-DD-YYYY	Relevant Portion	T <sup>6</sup>
		JP	3420984	B2	SANKYO CO., LTD.	4-18-2003		*
		JP	2000-297097	A	SANKYO CO., LTD.	10-24-2000		**
		JP	10-304889	A	IMANISHI	11-17-1998		**

Examiner Signature		Date Considered	
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\* EXAMINER: Initial if document considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number. <sup>2</sup> See kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Place a check here if English translation is attached.

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PTO/SB/08B (08-00)

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Substitute for Form 1449A/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				Application Number	10/577,982
				Filing Date	May 2, 2006
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				Group Art Unit	
				Examiner Name	
Sheet	2	of	3	Attorney Docket Number	06189/HG
<b>OTHER DOCUMENTS - NON-PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	Include name of author (in CAPITAL LETTERS), title of article, title of item, date, page(s), volume-issue number(s), publisher, city and/or country where published			T <sup>2</sup>
		Leonid KRUGLYAK, "Prospects for whole-genome linkage disequilibrium mapping of common disease genes," <u>Nature Genetics</u> , vol. 22, June 1999, pp. 139-144.  Henry A. ERLICH et al., "Recent Advances in the Polymerase Chain Reaction," <u>Science</u> , June 21, 1999, Vol. 252, pp. 1643-1651.  Koji MORITA et al., "Synthesis and Properties of 2'-O,4'-C-Ethylene-Bridged Nucleic Acids (ENA) as Effective Antisense Oligonucleotides," <u>Bioorganic &amp; Medicinal Chemistry</u> , (2003), Vol. 11, pp. 2211-2226.  Koji MORITA et al., "2'-O,4'-C-Ethylene-Bridged Nucleic Acids (ENA): Highly Nuclease- Resistant and thermodynamically Stable Oligonucleotides for Antisense Drug," <u>Bioorganic &amp; Medicinal Chemistry Letters</u> , (2002), Vol. 12, pp. 73-76.  Kenneth J. LIVAK, "Allelic discrimination using fluorogenic probes and the 5' nuclease assay," <u>Genetic Analysis: Biomolecular Engineering</u> , (1999), Vol. 14, pp. 143-149.  Timothy MORRIS et al., "Rapid Reverse Transcription-PCR Detection of Hepatitis C Virus RNA in Serum by Using the TaqMan Fluorogenic Detection System," <u>Journal of Clinical Microbiology</u> , Dec. 1996, Vol. 34, No. 12, pp. 2933-2936.  David LATORRA et al., "Enhanced Allele-specific PCR Discrimination in SNP Genotyping Using 3'Locked Nucleic Acid (LNA) Primers," <u>Human Mutations</u> , (2003), 22:79-85.  Peter MOURITZEN et al., "Single nucleotide polymorphism genotyping using locked nucleic acid (LNA™)," <u>Expert Rev. Mole. Diagn.</u> , (2003), 3, PP. 27-38.  David LATORRA et al., "Design considerations and effects of LNA in PCR primers," <u>Molecular and Cellular Probes</u> , (2003), 17, pp. 253-259.			
Examiner Signature				Date Considered	

\* EXAMINER: Initial if document considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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				Filing Date	May 2, 2006
				First Named Inventor	Makoto KOIZUMI
				Group Art Unit	
				Examiner Name	
Sheet	3	of	3	Attorney Docket Number	06189/HG
<b>OTHER DOCUMENTS - NON-PATENT LITERATURE DOCUMENTS</b>					
Examiner Initials <sup>1</sup>	Cite No. <sup>1</sup>	Include name of author (in CAPITAL LETTERS), title of article, title of item, date, page(s), volume-issue number(s), publisher, city and/or country where published			T <sup>2</sup>
		Björn TEWS et al., "Application of the C4'-Alkylated Deoxyribose Primer System (CAPS) in Allele-Specific Real-Time PCR for Increased Selectivity in Discrimination of Single Nucleotide Sequence Variants," <u>Biol. Chem.</u> , (2003) Vol. 384, pp. 1533-1541.  Makoto KOIZUMI et al., "Improvement of single nucleotide polymorphism genotyping by allele-specific PCR using primers modified with an ENA residue," <u>Analytical Biochemistry</u> , (2005), 340, pp. 287-294.  Makoto KOIZUMI et al., "SNP genotyping by allele-specific PCR using ENA primers," <u>Nucleic Acid Symposium Ser.</u> , (2005), No. 49, pp. 47-48.  Makoto KOIZUMI et al., "Triplex formation with 2'-O,4'-C-ethylene-bridged nucleic acids (ENA) having C3'-endo conformation at physiological pH," <u>Nucleic Acids Research</u> , (2003), Vol. 13, No. 12, pp. 3267-3273.  Koji MORITA et al., "2'-O,4'-C-Ethylene-Bridged Nucleic Acids (ENA): Highly Nuclease-Resistant and Thermodynamically Stable Oligonucleotides for Antisense Drug," <u>Bioorganic &amp; Medicinal Chemistry Letters</u> , (2002) 12, pp. 73-76.  Masafumi MATSUO et al., "Study of Ability of Antisense ENA to Induce Exon Skipping of Dystrophin Gene," Kosei Rodosho Seishin Shinkei Shikkan Kenkyu Itakuhi ni yoru Kenkyu Hokokushu, Heisei 14 Nendo, July 2003, p. 590.			*
Examiner Signature				Date Considered	

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